REMARKS

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 13-3402 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Respectfully submitted,

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MARKED UP VERSION TO SHOW CHANGES MADE

Marked up version of the paragraph starting at page 4, lines 16 to 25 is below:

The ED_b domain is a repetition sequence of type III that comprises 91 amino acids and has an extremely high sequence homology between the rat and chicken fibronectin, which is between 96% and 100%. No RGDS (SEQ ID NO: 5) sequences or other amino acid sequences occur within the domains, of which it is known that they mediate an interaction with integrins. The specific function of the ED-B domain is unknown up until now. Three studies have been published that conduct speculations on a general stimulating function with respect to adhesion/cell propagation for various cells.

Marked up version of the paragraph starting at page 6, line 17 through page 7, line 26 is below:

The study by Chen and Culp (1998, aaO) shows that the mono-repetition protein ED_b was more heavily promoted for the propagation of BALB/c 3T3 cells as well as for inducing FAK-tyrosine phosphorylation than the adjacent repeats III8, etc. The assumption is advanced that in the case of physiological concentrations of cellular fibronectins, the binding of the tetrapeptide RGDS (SEQ ID NO: 5) from III10 to the integrins possibly produces a signal of inadequate strength for the cell adhesion, so that no tyrosine-phosphorylation response arises from the interaction between III10 and integrin-mediated mechanisms. It is further assumed that the difference with respect to the response to the various mediated cell adhesions is produced by a varying activation of various small GTP-binding proteins. Three of these proteins -- cdc42, rac and rho -- which all are members of the ras-superfamily, play important roles in the case of cell-morphological changes. cdc42 acts sequentially upstream from rac and directly induces the appearance of filopodia (Nobes, C. D. and Hall, A., 1995, Rho, rac and cdc42 GTPa-ses Regulate the Assembly of Multimolecular Focal Complexes Associated with Actin Stress Fibers, Lamellipodia and Filopodia, **Cell. 81**, 53-62). The activation of rac is then responsible for the formation of lamellipodia and the network of actin filaments between the filopodia. Further downstream, rho can be activated by rac and induces focal adhesion and actin stress fibers. All of these events depend on the activation of tyrosine kinase, and it is assumed from FAK that it is involved in these processes. Chen and Culp

make the conjecture that the morphological differences between cells that are adherent via 7-ED_b-8 as well as cells that are adherent via 8-9-10 are based on the varying activation of the small GTP-binding proteins. The above suggests that an adhesion via 8-9-10 via the integrin-mediated signal path finally leads to an activation of rho to produce focal adhesions and actin stress fibers, while the adhesion of BALB/c-3T3 cells via 7-ED_b-8 leads only to an activation of cdc42 proteins and rac proteins, but does not activate rho. For the above-mentioned speculations, however, data are presented in neither of the two studies.

Marked up version of the paragraph starting at page 20, lines 24 to 25 is below:

Fig. 6 shows the partial sequences of synthetic peptides (SEQ ID NOS 4, 6-8, 1, 9-18, 2-3, 19-22, respectively in order of appearance) from the ED_b-fibronectin domains used in Fig. 5;

Marked up version of the paragraph starting at page 28, lines 8 to 11 is below:

Fig. 6 shows the partial sequences of the synthetic ED-B peptides (SEQ ID NOS 4, 6-8, 1, 9-18, 2-3, 19-22, respectively in order of appearance) with the selected sequence designations that are removed from the total sequence of the ED_b-fibronectin domains. The one-character code for amino acids is used.